eCTD Module 1 Version 2.3 (DTD v3.3) REMS 1.16 Heading

The following are instructions to assist applicants on where to place documents under the eCTD Module 1 REMS 1.16 sub-headings using DTD v3.3 of the us-regional.xml file.

1.16 Risk Management Plan

1.16.1 Risk Management (Non-REMS)

Applicants should place risk management plans (RMP), risk minimization action plans (RiskMAPs), and RiskMAP reports under this heading. Submission of a Risk Evaluation and Mitigation Strategy (REMS) should ***not*** be placed under this heading as REMS are to be included under heading 1.16.2. However, if the applicant is submitting a rationale for not submitting a proposed REMS, it should be placed here.

1.16.2 Risk Evaluation and Mitigation Strategy (REMS)

Do not include any files under this heading. The files should be specific for the lowest level of the hierarchy outlined in the FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy* available on our eCTD Web page[1] and provided below for sub-heading 1.16.2.

1.16.2.1 Final REMS

The final REMS document with all appended materials in their final format and the REMS supporting document (for original REMS, REMS modifications, and REMS revisions[2]) should be submitted in Microsoft Word and PDF format.

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[1] Table of Contents for eCTD: (http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM163175.pdf

[2] See draft Guidance for Industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions,* available at*:* *https://www.fda.gov/Drugs/GuidancecomplianceRegulatoryInformation/Guidances/default.htm*

1.16.2.2 Draft REMS

The proposed REMS document, all appended materials, and the REMS supporting document in clean and track changes for original REMS, REMS modifications, and REMS revisions should be submitted in Microsoft Word format as individual files. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

1.16.2.3 REMS Assessment

Applicant's REMS assessment report, abbreviated REMS assessment for an efficacy supplement, and responses to FDA "Requests for Information or Comments," that are associated with an assessment should be placed here.

1.16.2.4 REMS Assessment Methodology

Any survey or other methodology used to assess the REMS should be placed here.

1.16.2.5 REMS Correspondence

Official REMS related correspondence to the FDA that is not associated with a submission under review be placed here. Applicants' responses to FDA "Requests for Information or Comments," that are associated with a REMS supplement or an assessment that is under review should be included under applicable sub-headings.

1.16.2.6 REMS Modification History

It is recommended that applicants submit a REMS history that summarizes all type of changes (revisions, minor modifications, and major modifications) made to the REMS since its approval. [4] The REMS history should be in tabular format similar to the labeling history and submitted as a single PDF file.[5]

[4] See draft Guidance for Industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions,* available at*: https://www.fda.gov/Drugs/GuidancecomplianceRegulatoryInformation/Guidances/default.htm* for a more detailed description of the REMS history.

[5] eCTD Technical Conformance Guide: http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM465411.pdf